

Purpose/Objective: Rotational IMRT (rIMRT, tradenames VMAT(R), RapidArc(R)) has set new standards for the speed of treatment delivery. However, today's treatment machines are not optimized for this kind of delivery, with the consequence that design constraints on leaf and gantry rotation speeds and dose rates limit the achievable treatment times. Here, we explore the questions of how a specialized linac for rIMRT would have to be designed, and which treatment times are ideally achievable without loss of plan quality, relative to the best dose distributions achievable today.

Materials and Methods: The fundamental design of the hypothetical linac comprises: a continuously rotating gantry with a cone beam and a conventional MLC, a continuously variable dose rate with instantaneous beam switching, and a fixed patient position. Variable parameters were leaf and gantry rotation speed as well as maximum and minimum dose rate. The linac was modelled in a research version of a commercial TPS, being capable of rIMRT planning including segment shape optimization (direct aperture optimization). The leaf sequencing algorithm was specifically developed for this virtual linac, and determines the optimum leaf trajectories from the minimization of a complex cost function which comprises the input from multiple gantry angles simultaneously. It also finds the required number of full rotations. Planning studies were performed on cases of variable complexity to determine the combination of leaf and gantry speed which allows for the shortest delivery times.

Results: There appear to be two fundamentally different paths towards fast delivery times: for a slow moving gantry, fast leaves are obviously an advantage to increase the modulation per sector of the gantry rotation, because treatments with few full rotations are favoured. The other mode is an extremely fast rotating gantry (10-20 RPM), combined with a larger number of rotations and relatively low modulation per sector of the gantry rotation. Modulation is then achieved by multiple passes of the beam over the same sector. Both methods are capable of delivering the high quality of treatment plan possible with a modern state-of-the-art linac (reference plans were 2-arc plans for Varian TrueBeam(R) and Elekta Agility(R) linacs). Lower treatment times were achievable with the fast gantry rotation. The minimum was obtained at around 20 RPM/18 seconds for prostate cases, and 12 RPM/45 seconds for complex head-and-neck cases with 3 dose levels. Optimum max dose rates were 1200-1800 MU/min. Even faster gantry speed resulted in a greater number of beam interrupts and larger sectors of gantry rotation 'in the dark' and therefore more full rotations for realistic leaf speeds.

Conclusions: A planning study for a hypothetical, yet realistic, continuously rotating linac design with a novel type of leaf sequencing algorithm shows, that today's quality of dose distribution can be achieved with delivery times in the order of 20-45 seconds.

SYMPOSIUM: DOSE-DENSITY IN LUNG CANCER

SP-0288

Dose-fractionation in SBRT, the evolution towards central lesions

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The advent of SBRT for lung tumors has opened new horizons in the curative radiotherapy of lung cancer. In peripheral lesions, very high local control rates have throughout been reported after high dose hypofractionated radiotherapy. Besides high precision and small volumes, extreme treatment acceleration is a key feature for this success.

Therefore it is tempting to translate the successful concept of SBRT to more central lesions. However, while peripheral lesions are mainly surrounded by lung, the normal tissue neighborhood of central lesions is challenging and reports of severe and fatal normal tissue toxicities like bleedings and necroses have caused concerns.

On the other sides some patient cohorts with encouraging results after SBRT of central lesions have been observed after the use of less hypofractionated SBRT strategies raising the question of "overkill" by other dose/fractionation regimes.

In order to approach this issue scientifically, clinical studies are needed to prospectively assess not only local control but also toxicity. Current study concepts will be discussed.

SP-0289

Dose-escalation in LA NSCLC: Biological and technical aspects

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Experimental and clinical evidence for time-dose-fractionation in locally advanced non-small cell lung cancer as the basis for dose-escalation will be reviewed and strategies to improve outcome after radiotherapy will be discussed. An essential component of these strategies represents advanced technology in planning and treatment delivery such as motion management, image-guidance and functional imaging.

SP-0290

Optimal time-dose-fractionation in SCLC

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Optimising the management of patients with LDSCC continues to be a challenge. The relevant role of radiotherapy was clearly demonstrated in the early 1990's with two meta-analyses which established a survival benefit for patients treated with radio-chemotherapy, however, the optimal method of integrating thoracic radiotherapy (TRT) with chemotherapy remained undefined.

To date, some topics are still controversial: the optimal timing of radiotherapy, the radiation dose, the fractionation and the combined chemotherapy regimen.

The rationale for an early administration of radiation therapy during the course of chemotherapy may be to eliminate localized populations of chemotherapy-resistant tumour cells that might be responsible for treatment failure if permitted to disseminate systemically. This would be an obvious advantage of early administration of radiotherapy. Of the seven randomized controlled trials examining timing, only those with early chemoradiation have 5-year survival rates in excess of 20%. The "chemoradiation package" can be defined as the time from the start of chemotherapy until the completion of radiotherapy. The best median survival and long-term survival rates have been observed in trials with a chemoradiation package time of less than 6 weeks.

Several phase III trials investigated the timing and sequencing of radiotherapy. Fried et al. reported a meta-analysis carried out regarding the timing of radiotherapy. Six out of seven randomised trials, with a total of 1524 patients, favoured the use of early radiotherapy, and the overall risk ratio at 2 years was 1,17 (95%CI 1,02- 1,35; p=0,03) favouring the use of early radiotherapy. The subgroup analysis revealed that the benefit of the early radiotherapy schedule was seen in patients receiving hyperfractionated radiation and/or platinum based compared chemotherapy (18% of absolute benefit).

More recently, a significant relationship between the value of the time lapse from the first day of chemotherapy to the end of thoracic radiotherapy (SER), as well as overall survival and disease free survival, was reported. The analysis on 212 patients with limited stage SCLC shows that each day of extension of the SER resulted in increased probability of death (decrease of OS) by 0.28% and an increase of the risk of development failure (decrease of DFS) by 0.31%.

Historically, total doses of 40-50 Gy delivered in 1,8-2,0 Gy daily fractionation have been utilized in once daily radiation schemes. Clinical results comparing standard fractionation (SF) with total doses less than 54Gy and more than 54Gy or accelerated fractionation (AHF) show that for the local control rates, the overall and progression-free survival rates, all outcomes were significantly lower in the SF <54 Gy group than in the other two groups, although no significant difference was found between the AHF and SF ≥54 Gy groups.

With regard to fractionation, the customary once daily radiotherapy dose divided into two treatments each day has biologic advantages. In vitro, small-cell lung-cancer cell lines have marked radio-sensitivity even to small doses of radiation. The cornerstone trial is certainly Turrisi's one, an intergroup phase III study, in which accelerated hyperfractionation was superior to standard fractionation. At the five year follow-up, the difference between the treatments favoured the twice-daily treatment group by 10 percent in comparison with standard fractionation. As expected, esophageal toxicity was increased (G3 27% vs 11%, respectively).

More recently, a meta-analysis on modified fractionation on 685 patients with a median follow-up of 12.1 years and 622 deaths was published. The effect of modified RT on overall survival was absolute benefit of 1.7% at 3 years (from 29.6% to 31.3%) and 5.1% at 5 years (from 18.7% to 23.8%).

Only carefully conducted prospective clinical trials will allow us to further improve local control and survival rates of LD-SCLC patients in the future.

SP-0291

Normal tissue tolerance or optimal techniques

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